Literature update week 23 (2019)

[1] *Naydenov Naydenov S, Margaritov Runev N, Ivanov Manov E, Georgieva Torbova-Gigova S*. **EFFICACY AND SAFETY OF A SINGLE-PILL COMBINATION OF ATORVASTATIN/AMLODIPINE IN PATIENTS WITH ARTERIAL HYPERTENSION AND DYSLIPIDEMIA**. Acta clinica Croatica 2018; 57:464-472.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31168179
ABSTRACT
- The aim was to evaluate the efficacy of a single-pill combination of atorvastatin/amlodipine in patients with arterial hypertension, dyslipidemia and moderate to high cardiovascular risk. This prospective study included 243 patients with arterial hypertension, dyslipidemia and moderate to high cardiovascular risk, mean age 63.3+/-9.8 years. All patients were prescribed a treatment with one of the following doses of a single-pill combination of atorvastatin/amlodipine: 10/5, 10/10, 20/5 or 20/10 mg daily. The follow-up period was 3 months. The mean baseline values of the systolic and diastolic blood pressure were 155.7+/-16.2 and 92.0+/-9.2 mm Hg, respectively. At month 3, the respective mean systolic and diastolic blood pressure values were 136.9+/-26.9 and 80.6+/-5.1 mm Hg. The mean baseline values of total cholesterol and low-density lipoprotein cholesterol were 6.6+/-1.2 and 4.4+/-1.1 mmol/L, respectively. At month 3, the respective mean values of total cholesterol and low-density lipoprotein cholesterol were 5.1+/-0.9 and 2.9+/-1.0 mmol/L. Treatment was discontinued in 9 (3.7%) patients due to adverse events. In conclusion, treatment with the single-pill combination of atorvastatin/amlodipine was effective and well tolerated by the patients with arterial hypertension, dyslipidemia and moderate to high cardiovascular risk.

[2] *Sawrey-Kubicek L, Zhu C, Bardagjy AS et al.* **Whole egg consumption compared with yolk-free egg increases the cholesterol efflux capacity of high-density lipoproteins in overweight, postmenopausal women**. The American journal of clinical nutrition 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31172172
ABSTRACT
BACKGROUND: Postmenopausal women are at higher risk for cardiovascular disease (CVD) than their younger counterparts. HDL cholesterol is a biomarker for CVD risk, but the function of HDL may be more important than HDL cholesterol in deciphering disease risk. Although diet continues to be a cornerstone of treatment and prevention of CVD, little is known about how diet affects the functionality of HDL. OBJECTIVES: The aim of this study was to characterize the effects of whole eggs compared with yolk-free eggs on HDL function and composition in overweight, postmenopausal women and determine how changes in HDL composition are related to HDL functional parameters. METHODS: The study was a 14-wk, single-blind, randomized crossover dietary trial with two 4-wk intervention periods in 20 overweight, postmenopausal women. The crossover treatments were frozen breakfast meals containing 100 g of liquid (approximately 2) whole eggs compared with 100 g of (approximately 2) yolk-free eggs per day, separated by a 4-wk washout. Fasting blood samples were taken at the beginning and end of each treatment period to determine the effects on HDL composition and function. RESULTS: Cholesterol efflux capacity increased in the whole-egg treatment (mean +/- SD percentage change: +5.69% +/- 9.9%) compared with the yolk-free egg treatment (-3.69% +/- 5.3%) ($P < 0.01$), but there were no other significant changes in HDL functions or antioxidant or inflammatory markers. ApoA-I, total cholesterol (TC), LDL cholesterol, and HDL cholesterol also

did not change in response to the egg treatment. CONCLUSIONS: The consumption of 2 whole eggs/d by overweight, postmenopausal women showed a significant increase in cholesterol efflux capacity. This increase in cholesterol efflux capacity was seen without significant changes in apoA-I, TC, LDL cholesterol, or HDL cholesterol, supporting the idea that HDL function rather than HDL cholesterol should be addressed in this population. This trial was registered at clinicaltrials.gov as NCT02445638.

[3] *Bazerbachi F, Conboy EE, Mounajjed T et al.* **Cryptogenic Cirrhosis and Sitosterolemia: A Treatable Disease If Identified but Fatal If Missed**. Annals of hepatology 2017; 16:970-978.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31171340
ABSTRACT
Sitosterolemia is an autosomal recessive metabolic disease caused by mutations in ABCG5 or ABCG8 genes which encode for the (ATP)-binding cassette (ABC) transporters that are responsible for the trafficking of xenosterols. Liver involvement is not a recognized manifestation of this disease, and cirrhosis has been reported only once in the medical literature. We describe a fatal case of a 21-year old South Asian male who presented with decompensated cirrhosis, and biochemical abnormalities consistent with sitostero-lemia. Genetic testing showed a homozygous pathogenic mutation in ABCG5, confirming the diagnosis. Sitosterolemia is a rare, but likely under-recognized condition, and a high degree of suspicion is imperative to make the diagnosis. We propose that sitosterolemia should be included in the differential diagnosis for patients with cryptogenic cirrhosis, especially as there are effective oral therapies to treat this condition. Newly diagnosed sitosterolemia patients should undergo a thorough hepatology evaluation and follow-up to evaluate for the presence, development, and progression of any hepatic involvement.

[4] *Monrroy-Bravo H, Angulo J, Pino K et al.* **Effect of ezetimibe in HCV viral load after liver transplantation**. Annals of hepatology 2016; 15:803-805.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31155088
ABSTRACT

[5] *Shu S, Zhang Y, Li W et al.* **The role of monocyte chemotactic protein-induced protein 1 (MCPIP1) in angiotensin II-induced macrophage apoptosis and vulnerable plaque formation**. Biochem Biophys Res Commun 2019; 515:378-385.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31155290
ABSTRACT
Atherosclerotic plaque rupture is the main cause of acute coronary syndrome (ACS). Angiotensin II (Ang II) and macrophage apoptosis are involved in the pathogenesis of atherosclerosis. However, the underlying mechanisms remain unclear. We aimed to address the role of monocyte chemotactic protein-induced protein 1 (MCPIP1) in Ang II-induced macrophage apoptosis and vulnerable plaque formation. In mouse peritoneal macrophages, Ang II promoted endoplasmic reticulum (ER) stress-dependent macrophage apoptosis. Ang II markedly upregulated the expression of MCPIP1 via activating p38 mitogen-activated protein kinase (p38MAPK). Treatment with MCPIP1 shRNA downregulated ER stress-related proteins and decreased macrophage apoptosis induced by Ang II. Ang II also activated the AMP-

activated protein kinase (AMPK) signaling in macrophages. Inhibition of AMPK reduced macrophage apoptosis by inhibiting the p38MAPK/MCPIP1/ER stress pathway. Furthermore, blocking the Ang II type 1 receptor (AT1R) with losartan effectively inhibited Ang II-induced macrophage apoptosis and AMPK/p38MAPK/MCPIP1/ER pathway activation. In the atherosclerotic vulnerable plaque model in mice, losartan inhibited the progression of atherosclerosis and transformed vulnerable plaque into a more stable phenotype. Moreover, losartan markedly decreased the number of CD68(+)TUNEL(+), CD68(+)MCPIP1(+), CD68(+)p-eIF2alpha(+) and CD68(+)CHOP(+) cells in the lesion area. Taken together, Ang II promotes macrophage apoptosis via the AMPK/p38MAPK/MCPIP1/ER stress pathway in macrophages via its receptor AT1R, which may contribute to vulnerable plaque formation. Our study clarifies a novel regulatory role of MCPIP1 in Ang II-induced macrophage apoptosis and plaque instability, providing a potential therapeutic target for prevention of ACS.

[6] *Nogueira AA, Strunz CM, Takada JY, Mansur AP*. **Biochemical markers of muscle damage and high serum concentration of creatine kinase in patients on statin therapy**. Biomarkers in medicine 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31157560
ABSTRACT
Aim: Some patients experience statin-associated muscle symptoms (SAMS) and elevated serum concentrations of creatine kinase (CK). The relationship between SAMS and biomarkers of muscle damage was examined. Methods: We analyzed 359 consecutive patients taking statins with high CK values. Muscle-related symptoms and biochemical variables, including CK, MB isoenzyme of creatine kinase (CK-MB), troponin and carbonic anhydrase type III were evaluated. Results: SAMS was reported by 181 (50.4%) patients and they had greater BMI (p = 0.021) and a trend toward higher CK-MB values (p = 0.064). The use of simvastatin (OR: 2.24; 95% CI: 1.47-3.42), CK-MB (OR: 1.59; 95% CI: 1.02-2.49) and BMI (OR: 1.06; 95% CI: 1.01-1.10) were independent variables for SAMS. Conclusion: Simvastatin use, BMI and CK-MB were independent markers of SAMS.

[7] *Redmond P, McDowell R, Grimes TC et al.* **Unintended discontinuation of medication following hospitalisation: a retrospective cohort study**. BMJ open 2019; 9:e024747.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31167862
ABSTRACT
OBJECTIVES: Whether unintended discontinuation of common, evidence-based, long-term medication occurs after hospitalisation; what factors are associated with unintended discontinuation; and whether the presence of documentation of medication at hospital discharge is associated with continuity of medication in general practice. DESIGN: Retrospective cohort study between 2012 and 2015. SETTING: Electronic records and hospital supplied discharge notifications in 44 Irish general practices. PARTICIPANTS: 20 488 patients aged 65 years or more prescribed long-term medication for chronic conditions. PRIMARY AND SECONDARY OUTCOMES: Discontinuity of four evidence-based medication drug classes: antithrombotic, lipid-lowering, thyroid replacement drugs and respiratory inhalers in hospitalised versus non-hospitalised patients; patient and health system factors associated with discontinuity; impact of the presence of medication in the hospital discharge summary on

continuity of medication in a patient's general practitioner (GP) prescribing record at 6 months follow-up. RESULTS: In patients admitted to hospital, medication discontinuity ranged from 6%-11% in the 6 months posthospitalisation. Discontinuity of medication is significantly lower for hospitalised patients taking respiratory inhalers (adjusted OR (AOR) 0.63, 95% CI (0.49 to 0.80), p<0.001) and thyroid medications (AOR 0.62, 95% CI (0.40 to 0.96), p=0.03). There is no association between discontinuity of medication and hospitalisation for antithrombotics (AOR 0.95, 95% CI (0.81 to 1.11), p=0.49) or lipid lowering medications (AOR 0.92, 95% CI (0.78 to 1.08), p=0.29). Older patients and those who paid to see their GP were more likely to experience increased odds of discontinuity in all four medicine groups. Less than half (39% to 47.4%) of patients had medication listed on their hospital discharge summary. Presence of medication on hospital discharge summary is significantly associated with continuity of medication in the GP prescribing record for lipid lowering medications (AOR 1.64, 95% CI (1.15 to 2.36), p=0.01) and respiratory inhalers (AOR 2.97, 95% CI (1.68 to 5.25), p<0.01). CONCLUSION: Discontinuity of evidence-based long-term medication is common. Increasing age and private medical care are independently associated with a higher risk of medication discontinuity. Hospitalisation is not associated with discontinuity but less than half of hospitalised patients have medication recorded on their hospital discharge summary.

[8] *Fruchart JC, Santos RD, Aguilar-Salinas C et al.* **The selective peroxisome proliferator-activated receptor alpha modulator (SPPARMalpha) paradigm: conceptual framework and therapeutic potential : A consensus statement from the International Atherosclerosis Society (IAS) and the Residual Risk Reduction Initiative (R3i) Foundation**. Cardiovascular diabetology 2019; 18:71.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31164165
ABSTRACT
In the era of precision medicine, treatments that target specific modifiable characteristics of high-risk patients have the potential to lower further the residual risk of atherosclerotic cardiovascular events. Correction of atherogenic dyslipidemia, however, remains a major unmet clinical need. Elevated plasma triglycerides, with or without low levels of high-density lipoprotein cholesterol (HDL-C), offer a key modifiable component of this common dyslipidemia, especially in insulin resistant conditions such as type 2 diabetes mellitus. The development of selective peroxisome proliferator-activated receptor alpha modulators (SPPARMalpha) offers an approach to address this treatment gap. This Joint Consensus Panel appraised evidence for the first SPPARMalpha agonist and concluded that this agent represents a novel therapeutic class, distinct from fibrates, based on pharmacological activity, and, importantly, a safe hepatic and renal profile. The ongoing PROMINENT cardiovascular outcomes trial is testing in 10,000 patients with type 2 diabetes mellitus, elevated triglycerides, and low levels of HDL-C whether treatment with this SPPARMalpha agonist safely reduces residual cardiovascular risk.

[9] *Arnold SV, de Lemos JA, Rosenson RS et al.* **Use of Guideline-Recommended Risk-Reduction Strategies Among Patients with Diabetes and Atherosclerotic Cardiovascular Disease: Insights from Getting to an Improved Understanding of Low-Density Lipoprotein Cholesterol and Dyslipidemia Management (GOULD)**. Circulation 2019.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31174429

ABSTRACT

Patients with atherosclerotic cardiovascular disease (ASCVD) and concomitant diabetes are at particularly high risk for new and recurrent ischemic events and heart failure and therefore derive greater absolute benefit from secondary prevention therapies than patients without concomitant diabetes.(1) Prior analyses reported suboptimal use of evidence-based therapies in this vulnerable group(1, 2) but did not include data on newer lipid and glucose-lowering therapies. Given the emergence of non-statin LDL lowering agents and glucose-lowering medications with cardiovascular benefits, the number of evidence-based therapies for secondary prevention has expanded. Thus, we examined contemporary use of medications to reduce cardiovascular risk in a large cohort of US patients with diabetes and ASCVD.

[10] *Thurmann PA, Kleineruschkamp AG, Boehme P*. **[The Polypill - A Practicable Approach?]**. Deutsche medizinische Wochenschrift (1946) 2019; 144:715-718.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31163467

ABSTRACT

Polypills used in cardiovascular prevention contain combinations of aspirin, lipid-lowering drugs and blood pressure-lowering drugs. The use of polypills can improve adherence while physicians express concerns about therapy safety and flexibility.

[11] *Chatterjee D, Kapoor A, Vijay S et al.* **Efficacy of Locally Administered 1.2% Rosuvastatin Gel in Patients with Periodontitis: A Randomized Placebo Controlled Clinical Trial**. European journal of dentistry 2019; 13:29-35.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31170754

ABSTRACT

OBJECTIVE: Periodontitis initiation and progression are a result of host immune inflammatory response to oral pathogens. Several pharmacological agents are being delivered locally, to improve periodontal health. Hence, the present randomized placebo controlled clinical trial is designed to check the clinical and antimicrobial efficacy of locally delivered 1.2% rosuvastatin (RSV) in intrabony defects (IBD) in periodontitis patients. MATERIALS AND METHODS: One-hundred patients were randomly allotted into two treatment groups: group A received 1. 2% RSV gel, scaling and root debridement and group B received placebo gel, scaling and root debridement. Clinical parameters, including modified sulcus bleeding index (mSBI), probing depth (PD), clinical attachment level (CAL), and plaque index (PI), were recorded at baseline before phase 1 and after 6 months. Radiographic assessment of IBD was done by cone beam computed tomography at baseline and after 6 months. Anaerobic colony count was done at baseline and after 180 days. RESULTS: On intragroup comparison, there is a significant improvement in periodontal parameters in both the groups. On intergroup comparison, there is significant gain in CAL in group A than group B ($p = 0.04$). There is significant decrease in PD in group A, compared to group B. There is significant bone fill in group A ($p = 0.034$), compared to group B. With respect to mSBI, PI, and anaerobic colony count, there is no significant difference between the two groups after 6 months. No adverse effect was noticed in any subjects. CONCLUSION: The author concludes that 1.2% RSV gel when delivered locally into IBD improved periodontal clinical parameters such as PD and CAL and showed significant bone fill.

[12] *Barber CN, Raben DM*. **Lipid Metabolism Crosstalk in the Brain: Glia and Neurons**. Frontiers in cellular neuroscience 2019; 13:212.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31164804
ABSTRACT
Until recently, glial cells have been considered mainly support cells for neurons in the mammalian brain. However, many studies have unveiled a variety of glial functions including electrolyte homeostasis, inflammation, synapse formation, metabolism, and the regulation of neurotransmission. The importance of these functions illuminates significant crosstalk between glial and neuronal cells. Importantly, it is known that astrocytes secrete signals that can modulate both presynaptic and postsynaptic function. It is also known that the lipid compositions of the pre- and post-synaptic membranes of neurons greatly impact functions such as vesicle fusion and receptor mobility. These data suggest an essential lipid-mediated communication between glial cells and neurons. Little is known, however, about how the lipid metabolism of both cell types may interact. In this review, we discuss neuronal and glial lipid metabolism and suggest how they might interact to impact neurotransmission.

[13] *Cheng S, Wu Y, Wen W et al.* **Independent Severe Cases of Heterozygous Familial Hypercholesterolemia Caused by the W483X and Novel W483G Mutations in the Low-Density Lipoprotein Receptor Gene That Were Clinically Diagnosed as Homozygous Cases**. Genetic testing and molecular biomarkers 2019; 23:401-408.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31161821
ABSTRACT
Background and Aims: The genetic spectrum underlying familial hypercholesterolemia (FH) remains unclear, especially in northeastern China. The aim of this study was to delineate the FH genetic spectrum and identify specific characteristics of FH patients in this region. Materials and Methods: The family history, personal medical history, and lifestyle habits of two unrelated patients clinically diagnosed with homozygous FH were recorded. DNA samples of the patients and their relatives were subjected to a newly designed next-generation sequencing panel using an Illumina Miseq platform. Detected variants were annotated and functionally predicted with in silico algorithms, and protein structures were modeled. Results: The patients' cholesterol levels were effectively reduced to 33.8% and 17.2% of the original level under conventional ezetimibe and statin treatment. Two pathogenic mutations, W483X and the novel mutation W483G, in the low-density lipoprotein receptor (LDLR) gene were identified. Both patients were heterozygous for the respective mutations. Under a high cholesterol/carbohydrate diet, these mutations could trigger a severe FH phenotype, but both patients responded well to regular medical treatments and dietary control. The W483X mutation results in a premature stop codon, leading to incomplete protein formation. Although the W483G mutation results in translation of the complete protein with no apparent structural difference, it still led to a severe FH phenotype similar to W483X. Conclusions: Identification of the novel W483G mutation expands the genetic spectrum of FH. Both mutations cause a severe FH phenotype under certain conditions, suggesting that W483 is important for LDLR function, highlighting potential targets for genetic screening or drug development.

[14] *Ayala Solares JR, Canoy D, Raimondi FED et al.* **Long-Term Exposure to Elevated Systolic Blood Pressure in Predicting Incident Cardiovascular Disease: Evidence From Large-Scale Routine Electronic Health Records**. Journal of the American Heart Association 2019; 8:e012129.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31164039

ABSTRACT

Background How measures of long-term exposure to elevated blood pressure might add to the performance of "current" blood pressure in predicting future cardiovascular disease is unclear. We compared incident cardiovascular disease risk prediction using past, current, and usual systolic blood pressure alone or in combination. Methods and Results Using data from UK primary care linked electronic health records, we applied a landmark cohort study design and identified 80 964 people, aged 50 years (derivation cohort=64 772; validation cohort=16 192), who, at study entry, had recorded blood pressure, no prior cardiovascular disease, and no previous antihypertensive or lipid-lowering prescriptions. We used systolic blood pressure recorded up to 10 years before baseline to estimate past systolic blood pressure (mean, time-weighted mean, and variability) and usual systolic blood pressure (correcting current values for past time-dependent blood pressure fluctuations) and examined their prospective relation with incident cardiovascular disease (first hospitalization for or death from coronary heart disease or stroke/transient ischemic attack). We used Cox regression to estimate hazard ratios and applied Bayesian analysis within a machine learning framework in model development and validation. Predictive performance of models was assessed using discrimination (area under the receiver operating characteristic curve) and calibration metrics. We found that elevated past, current, and usual systolic blood pressure values were separately and independently associated with increased incident cardiovascular disease risk. When used alone, the hazard ratio (95% credible interval) per 20-mm Hg increase in current systolic blood pressure was 1.22 (1.18-1.30), but associations were stronger for past systolic blood pressure (mean and time-weighted mean) and usual systolic blood pressure (hazard ratio ranging from 1.39-1.45). The area under the receiver operating characteristic curve for a model that included current systolic blood pressure, sex, smoking, deprivation, diabetes mellitus, and lipid profile was 0.747 (95% credible interval, 0.722-0.811). The addition of past systolic blood pressure mean, time-weighted mean, or variability to this model increased the area under the receiver operating characteristic curve (95% credible interval) to 0.750 (0.727-0.811), 0.750 (0.726-0.811), and 0.748 (0.723-0.811), respectively, with all models showing good calibration. Similar small improvements in area under the receiver operating characteristic curve were observed when testing models on the validation cohort, in sex-stratified analyses, or by using different landmark ages (40 or 60 years). Conclusions Using multiple blood pressure recordings from patients' electronic health records showed stronger associations with incident cardiovascular disease than a single blood pressure measurement, but their addition to multivariate risk prediction models had negligible effects on model performance.

[15] *Kanukula R, Esam H, Sundstrom J et al.* **Does Co-administration of Antihypertensive Drugs and Statins Alter Their Efficacy and Safety? A Systematic Review and Meta-analysis of Randomized Controlled Trials**. Journal of cardiovascular pharmacology 2019; 73:352-358.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31162243

ABSTRACT

Antihypertensive drugs (AHTDs) and statins are frequently administered together, but there is uncertainty on whether the presence of one affects the main effects of the other. This systematic review and meta-analysis assessed the effects of co-administered AHTDs and statins on blood pressure (BP) and cholesterol. MEDLINE, Cochrane Central Register of Controlled Trials and drug regulatory agency websites were searched, until January 2018. Twelve double-blind randomized controlled trials that allocated adults with or without hypertension and/or hyperlipidemia (n = 4434) to fixed doses of AHTD alone, statin alone and both drugs together, for >/=4 weeks, were included. BP lowering was similar with AHTD + statin compared with AHTD alone [systolic BP -0.1 mm Hg, 95% confidence interval (CI), -1.0 to 0.8, and diastolic BP -1.0 mm Hg, 95% CI, -2.3 to -0.2]. AHTD + statin compared with statin alone resulted in small reduction in low-density lipoprotein cholesterol (-3.9 mg/dL, 95% CI, -6.1 to -1.7), and this effect was largely associated with co-administration of amlodipine and atorvastatin or rosuvastatin. There was no difference in safety outcomes. Overall, it can be concluded that there is no clinically important difference in the effects of AHTDs and statins whether used separately or together for reduction in BP and low-density lipoprotein cholesterol.

[16] *Muller-Wieland D, Rader DJ, Moriarty PM et al.* **Efficacy and Safety of Alirocumab 300 mg Every 4 Weeks in Individuals with Type 2 Diabetes on Maximally Tolerated Statin**. The Journal of clinical endocrinology and metabolism 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31166599
ABSTRACT
BACKGROUND: Individuals with diabetes and elevated LDL-C are at particularly high risk of atherosclerotic cardiovascular disease. ODYSSEY CHOICE I (NCT01926782) assessed alirocumab 300 mg every 4 weeks (Q4W) in patients with hypercholesterolemia. We evaluated alirocumab efficacy and safety in a patient subgroup with type 2 diabetes (T2DM) on maximally tolerated statins with/without other lipid-lowering therapies. METHODS: CHOICE I study participants received either alirocumab 300 mg Q4W (n=458, including 96 with T2DM) or placebo (n=230, including 50 with T2DM) for 48 weeks, with alirocumab dose adjustment to 150 mg Q2W at Week (W)12 if W8 LDL-C levels were >/=70/100 mg/dL, depending on cardiovascular risk, or if LDL-C reduction was <30% from baseline. Efficacy endpoints included percentage change from baseline to W24 for LDL-C and other lipids, and time-averaged LDL-C over W21-24. RESULTS: In individuals with T2DM, LDL-C reductions from baseline to W24 and average of W21-24 were significantly greater with alirocumab (-61.6% and -68.8% vs placebo, respectively). At W24, alirocumab also significantly reduced levels of non-HDL-C, apolipoprotein B, triglycerides, and lipoprotein (a). At W24, 85.9% (alirocumab) and 12.5% (placebo) of individuals reached both non-HDL-C <100 mg/dL and LDL-C <70 mg/dL. At W12, 18% of alirocumab-treated individuals received dose adjustment. Most common treatment-emergent adverse events were upper respiratory tract infection and injection-site reaction. No clinically significant changes in fasting plasma glucose and glycated hemoglobin were observed. CONCLUSIONS: In individuals with T2DM, alirocumab 300 mg Q4W dosing regimen is generally well tolerated and efficacious in reducing atherogenic lipoproteins represented by LDL-C and non-HDL-C.

[17] *Rannikko J, Jacome Sanz D, Ortutay Z et al.* **Reduced plasma PCSK9 response in patients with bacteraemia is associated with mortality**. Journal of internal medicine 2019.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31166632

ABSTRACT

BACKGROUND: The proprotein convertase subtilisin/kexin type 9 (PCSK9) enzyme controls blood cholesterol levels by downregulating the expression of the low-density lipoprotein receptor (LDLR). Pathogenic lipids (e.g. lipopolysaccharide) are removed from the circulation by an LDLR/PCSK9-dependent mechanism; thus, it has been suggested that PCSK9 inhibitors may be beneficial in the treatment of infections. We measured plasma PCSK9 levels in patients with culture-positive bacteraemia and explored pathogen-dependent and infection site-dependent effects as well as correlations between patient characteristics and outcome. METHODS: Proprotein convertase subtilisin/kexin type 9 in the plasma was measured with an enzyme-linked immunosorbent assay from 481 patients with blood culture-positive infection on days 0 to 4 after admission to the emergency department. Patient outcome and clinical and laboratory data were gathered retrospectively from patient records. RESULTS: The plasma PCSK9 level was elevated equally in patients with Gram-positive or Gram-negative bacterial infections; particularly high levels were seen in patients with a lower respiratory tract infection and Streptococcus pneumoniae bacteraemia. PCSK9 levels showed a significant positive correlation with C-reactive protein (CRP) level. Bacteraemia patients with liver disease or a history of alcohol abuse had significantly lower levels of plasma PCSK9. Reduced PCSK9 plasma responses in patients were significantly associated with mortality at days 7, 28 and 90. CONCLUSION: Proprotein convertase subtilisin/kexin type 9 is upregulated in blood culture-positive infections. Plasma PCSK9 resembles acute-phase proteins; its expression is induced during an infection, reduced in liver disease and correlates positively with CRP level. We have shown that PCSK9 levels are lower in patients with a fatal prognosis.

[18] *Shirouchi B, Matsuoka R*. **Alleviation of Metabolic Syndrome with Dietary Egg White Protein**. Journal of oleo science 2019; 68:517-524.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31168041

ABSTRACT

Abdominal fat accumulation causes metabolic syndrome, which is a cluster of metabolic abnormalities such as dyslipidemia, glucose intolerance, insulin resistance or hyperinsulinemia, and hypertension, leading to the development of diabetes and cardiovascular disease. Diets are known to contribute to the development or prevention of metabolic syndrome. Several studies have reported that the quality of dietary proteins may be an important modulator of the risk of this syndrome. We investigated the effects of consuming egg white protein (EWP) or lactic-fermented egg white (LE), an easy-to-consume form of egg white, on the development of metabolic syndrome in animal models and humans. In comparison with casein, dietary EWP decreased lymphatic lipid transport in thoracic lymph duct-cannulated rats. In an in vitro experiment, EWP pepsin hydrolysate decreased the cholesterol micellar solubility and cholesterol transfer rate from micelles to oil phase, and increased water-holding capacity, settling volume in water, and relative viscosity compared with casein pepsin hydrolysate. The daily consumption of LE for 8 weeks reduced serum total cholesterol and LDL cholesterol levels in men with mild hypercholesterolemia. Furthermore, dietary EWP reduced the body fat mass of rats by increasing the body protein mass and accelerating hepatic beta-oxidation. The daily consumption of LE for 12 weeks reduced the visceral fat area and improved the ratio of the

visceral to subcutaneous fat area. Taken together, these results indicated that dietary EWP and LE would be useful for preventing or alleviating metabolic syndrome.

[19] *Koivusalo A, Mutanen A, Nissinen M et al.* **Altered Bile Transporter Expression and Cholesterol Metabolism in Children with Cholesterol and Pigment Gallstones**. Journal of pediatric gastroenterology and nutrition 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31169656
ABSTRACT
OBJECTIVES.: We elucidated pathophysiology of pediatric gallstone disease by assessing liver expression of bile transporters in relation to bile acids and surrogates of cholesterol absorption and synthesis in serum and gallstones. METHODS.: RNA expression of canalicular bile transporters in liver biopsies from 32 pediatric gallstone patients and from six liver donors (controls) was measured by qRT-PCR. Concentrations of cholesterol and precursors, plant sterols and bile acids in gallstones, and in serum of the patients and 82 healthy children were measured. Primary outcomes were the difference in RNA expressions and serum sterol profiles between patients and controls. RESULTS.: Cholesterol stones (CS; n = 15) contained cholesterol >42% and pigment stones (PS; n = 17) <9% of weight. CS-patients had markedly lower serum plant sterols (absorption) and higher cholesterol precursors (synthesis) than PS-patients or healthy controls. CS contained several times more cholesterol precursors and less plant sterols relative to cholesterol than PS, which were enriched by primary bile acids (12-5.2 fold, $p<0.001$). Liver RNA expression of ABCG5/G8 was similarly increased 2.5-1.8 fold ($p < 0.002$) in CS and PS-patients, while PS-patients had higher ABCB11 expression ($p < 0.05$). In PS bile acid concentration correlated with gallstone plant sterols ($R = 0.83$, $p < 0.0001$), and ABCG5 expression with ACBC11 expression ($R2 = 0.27$, $p = 0.03$). CONCLUSIONS: In CS, upregulation of ABCG5/G8 expression associates with low absorption and high gallstone content of cholesterol. In PS, activation of bile acid transport by ACBC11 interconnects with hepatic upregulation of ABCG5/G8 enriching PS with bile acids and plant sterols.

[20] *Conte MS, Bradbury AW, Kolh P et al.* **Global vascular guidelines on the management of chronic limb-threatening ischemia**. Journal of vascular surgery 2019; 69:3S-125S.e140.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31159978
ABSTRACT
Chronic limb-threatening ischemia (CLTI) is associated with mortality, amputation, and impaired quality of life. These Global Vascular Guidelines (GVG) are focused on definition, evaluation, and management of CLTI with the goals of improving evidence-based care and highlighting critical research needs. The term CLTI is preferred over critical limb ischemia, as the latter implies threshold values of impaired perfusion rather than a continuum. CLTI is a clinical syndrome defined by the presence of peripheral artery disease (PAD) in combination with rest pain, gangrene, or a lower limb ulceration >2 weeks duration. Venous, traumatic, embolic, and nonatherosclerotic etiologies are excluded. All patients with suspected CLTI should be referred urgently to a vascular specialist. Accurately staging the severity of limb threat is fundamental, and the Society for Vascular Surgery Threatened Limb Classification system, based on grading of Wounds, Ischemia, and foot Infection (WIfI) is endorsed. Objective hemodynamic testing, including toe pressures as the preferred measure, is required to assess CLTI. Evidence-based

revascularization (EBR) hinges on three independent axes: Patient risk, Limb severity, and ANatomic complexity (PLAN). Average-risk and high-risk patients are defined by estimated procedural and 2-year all-cause mortality. The GVG proposes a new Global Anatomic Staging System (GLASS), which involves defining a preferred target artery path (TAP) and then estimating limb-based patency (LBP), resulting in three stages of complexity for intervention. The optimal revascularization strategy is also influenced by the availability of autogenous vein for open bypass surgery. Recommendations for EBR are based on best available data, pending level 1 evidence from ongoing trials. Vein bypass may be preferred for average-risk patients with advanced limb threat and high complexity disease, while those with less complex anatomy, intermediate severity limb threat, or high patient risk may be favored for endovascular intervention. All patients with CLTI should be afforded best medical therapy including the use of antithrombotic, lipid-lowering, antihypertensive, and glycemic control agents, as well as counseling on smoking cessation, diet, exercise, and preventive foot care. Following EBR, long-term limb surveillance is advised. The effectiveness of nonrevascularization therapies (eg, spinal stimulation, pneumatic compression, prostanoids, and hyperbaric oxygen) has not been established. Regenerative medicine approaches (eg, cell, gene therapies) for CLTI should be restricted to rigorously conducted randomizsed clinical trials. The GVG promotes standardization of study designs and end points for clinical trials in CLTI. The importance of multidisciplinary teams and centers of excellence for amputation prevention is stressed as a key health system initiative.

[21] *Fonarow GC, van Hout B, Villa G et al.* **Updated Cost-effectiveness Analysis of Evolocumab in Patients With Very High-risk Atherosclerotic Cardiovascular Disease**. JAMA cardiology 2019. **PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=31166576

ABSTRACT

Importance: In October 2018, evolocumab was made available at a reduced annual list price of $5850 in the United States. This 60% reduction was aimed at improving patient access by lowering patient copays. Shortly thereafter, the 2018 American College of Cardiology/American Heart Association cholesterol management guideline was released. An updated cost-effectiveness analysis of evolocumab in the United States may be therefore of interest to payers and prescribers. Objective: To present an updated cost-effectiveness analysis of evolocumab added to standard background therapy compared with standard background therapy alone in patients with very high-risk atherosclerotic cardiovascular disease, reflecting the 2018 ACC/AHA guideline definition and using the new evolocumab list price. Design, Setting, and Participants: This study used the Markov model originally used in a previous study by Fonarow et al in 2017. A US societal perspective was considered, and a range of baseline cardiovascular event rates were modeled to reflect varying risk profiles in clinical practice within patients with very high-risk atherosclerotic cardiovascular disease. Exposures: Addition of evolocumab to standard background therapy, including maximally tolerated statin therapy (ie, the maximum intensity of statin therapy a patient can safely receive), with or without ezetimibe. Main Outcomes and Measures: Major cardiovascular events (myocardial infarction, ischemic stroke, and cardiovascular death), costs, quality-adjusted life-years, and incremental cost-effectiveness ratios. Results: Evolocumab was associated with both increased costs and improved outcomes when added to standard background therapy. Incremental costs ranged

from $22228 to $3411, depending on the varying level of risk within the defined population. Incremental quality-adjusted life years ranged from 0.39 to 0.44. Incremental cost-effectiveness ratios ranged from $56655 to $7667 per quality-adjusted life-year gained. For a range of baseline cardiovascular event rates in patients with very high-risk atherosclerotic cardiovascular disease, incremental cost-effectiveness ratios were below the generally accepted willingness-to-pay thresholds. Moreover, the ratios were below the threshold of $50000 per quality-adjusted life-years gained for any baseline rate of 6.9 or more events per 100 patient-years. Conclusions and Relevance: At its current list price, the addition of evolocumab to standard background therapy meets accepted cost-effectiveness thresholds across a range of baseline cardiovascular event rates in patients with very high-risk atherosclerotic cardiovascular disease as defined by the 2018 ACC/AHA guideline.

[22] *Guillermier C, Doherty SP, Whitney AG et al.* **Imaging mass spectrometry reveals heterogeneity of proliferation and metabolism in atherosclerosis**. JCI insight 2019; 4.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31167964

ABSTRACT

Atherosclerotic plaques feature local proliferation of leukocytes and vascular smooth muscle cells (VSMCs) and changes in cellular metabolism. Yet the relationship between glucose utilization and proliferation has been technically impossible to study directly in cells of atherosclerotic plaques in vivo. We used multi-isotope imaging mass spectrometry (MIMS), a quantitative imaging platform, to measure coincident cell division and glucose utilization at suborganelle resolution in atherosclerotic plaques. In established plaques, 65% of intimal foam cells and only 4% of medial VSMCs were labeled with 15N-thymidine after 1 week of isotope treatment. Dividing cells demonstrated heightened glucose labeling. MIMS detected 2H-glucose label in multiple subcellular compartments within foam cells, including lipid droplets, the cytosol, and chromatin. Unexpectedly, we identified an intensely focal region of 2H-label in VSMCs underlying plaques. This signal diminished in regions of aorta without atherosclerosis. In advanced plaques, 15N-thymidine and 2H-glucose labeling in foam cells and VSMCs significantly decreased. These data demonstrate marked heterogeneity in VSMC glucose metabolism that was dependent on both proliferative status and proximity of VSMCs to plaques. Furthermore, these results reveal how quantitative mass spectrometry coupled with isotope imaging can complement other methods used to study cell biology directly in the growing atherosclerotic plaque in vivo.

[23] *Su X, Kong Y, Peng D*. **Evidence for changing lipid management strategy to focus on non-high density lipoprotein cholesterol**. Lipids in health and disease 2019; 18:134.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31170997

ABSTRACT

Low-density lipoprotein cholesterol (LDL-C) has been recommended as the primary treatment target on lipid management in coronary heart disease (CHD) patients for past several decades. However, even by aggressive LDL-C lowering treatment, patients still present a significant residual risk of major adverse cardiovascular events (MACE). Non-high-density lipoprotein cholesterol (non-HDL-C) contained all the atherogenic lipoproteins, such as chylomicron, very-low density lipoprotein (VLDL), LDL, intermediate density lipoprotein (IDL). Many prospective

observation studies have found that non-HDL-C was better than LDL-C in predicting risks of MACE. Since non-HDL-C appears to be superior for risk prediction beyond LDL-C, current guidelines have emphasize the importance of non-HDL-C for guiding cardiovascular prevention strategies and have flagged non-HDL-C as a co-primary therapeutic target. The goals of non-HDL-C were recommended as 30 mg/dl higher than the corresponding LDL-C goals, but the value seemed inappropriate. This review provide evidence for changing lipid management strategy to focus on non-HDL-C and appropriate values for adding to LDL-C goals would be proposed.

[24] *Chung SW, Lee JH, Kim MA et al.* **Additional fibrate treatment in UDCA-refractory PBC patients**. Liver international : official journal of the International Association for the Study of the Liver 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31162879
ABSTRACT
BACKGROUND & AIMS: There is no proven treatment for ursodeoxycholic acid (UDCA)-refractory primary biliary cholangitis (PBC) other than obeticholic acid. Although fibrates have been reported to improve biochemical parameters, the long-term effects remain unclear. This study evaluated the effect of fibrate on clinical outcomes of UDCA-refractory PBC. METHODS: Patients whose alkaline phosphatase (ALP) was not normalized with at least 13 mg/kg of UDCA treatment for >1 year were included from two tertiary referral centers. The primary outcome was ALP normalization. Secondary outcomes included the development of cirrhosis and hepatic deterioration. Immortal time bias was adjusted using the Mantel-Byar method. RESULTS: A total of 100 UDCA-refractory PBC patients were included: 71 patients received UDCA alone (the UDCA group) and 29 patients received UDCA plus additional fibrate treatment of 160 mg/day fenofibrate or 400 mg/day bezafibrate (the fibrate/UDCA group). During the follow-up period, the probability of ALP normalization was significantly higher in the fibrate/UDCA group [hazard ratio (HR)=5.00, 95% confidence interval=2.87-8.27, P<0.001]. Among 58 non-cirrhotic patients (43 in the UDCA group and 15 in the fibrate/UDCA group), 19 patients (44.1%) in the UDCA group and none in the fibrate/UDCA group developed cirrhosis (HR=0.12, P=0.04). Hepatic deterioration (Child-Pugh score increase or signs of decompensated cirrhosis) occurred in 17 patients (23.9%) of the UDCA group and none in the fibrate/UDCA group which the difference was significant (HR=0.12, P=0.04). CONCLUSIONS: In patients with UDCA-refractory PBC, additional fibrate treatment is associated with a higher probability of ALP normalization and a lower risk of cirrhosis development and hepatic deterioration.

[25] *Zhang S, Fu J, Zhang Q et al.* **Association between nut consumption and non-alcoholic fatty liver disease in adults**. Liver international : official journal of the International Association for the Study of the Liver 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31162803
ABSTRACT
BACKGROUND & AIMS: Increased nut consumption has been associated with reduced inflammation, insulin resistance, and oxidative stress. Although these factors are closely involved in the pathogenesis of non-alcoholic fatty liver disease (NAFLD), few studies have

focused on the association between nut consumption and NAFLD in the general population. We aimed to investigate the association of nut consumption and NAFLD in an adult population. METHODS: A total of 23 915 participants from Tianjin Chronic Low-Grade Systemic Inflammation and Health (TCLSIH) Cohort Study were included in this study. Information on dietary intake was collected using a validated food frequency questionnaire. Abdominal ultrasonography was done to diagnose NAFLD. Multivariable logistic regression was used to assess the association of nut consumption with NAFLD. RESULTS: After adjusting for sociodemographic, medical, dietary, and lifestyle variables, the odds ratios (95% confidence interval) for NAFLD across categories of nut consumption were 1.00 (reference) for <1 time/week, 0.91 (0.82, 1.02) for 1 time/week, 0.88 (0.76, 1.02) for 2-3 times/week, and 0.80 (0.69, 0.92) for >/=4 times/week (P for trend < 0.01). These associations were attenuated but remained significant after further adjustment for blood lipids, glucose, and inflammation markers. CONCLUSIONS: Higher nut consumption was significantly associated with lower prevalence of NAFLD. Further prospective studies and randomized trials are required to ascertain the causal association between nut consumption and NAFLD.

[26] *Ikebe Y, Ishimaru H, Imai H et al.* **Quantitative Susceptibility Mapping for Carotid Atherosclerotic Plaques: A Pilot Study**. Magnetic resonance in medical sciences : MRMS : an official journal of Japan Society of Magnetic Resonance in Medicine 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31155568

ABSTRACT

PURPOSE: Identifying plaque components such as intraplaque hemorrhage, lipid rich necrosis, and calcification is important to evaluate vulnerability of carotid atherosclerotic plaque; however, conventional vessel wall MR imaging may fail to discriminate plaque components. We aimed to evaluate the components of plaques using quantitative susceptibility mapping (QSM), a newly developed post-processing technique to provide voxel-based quantitative susceptibilities. METHODS: Seven patients scheduled for carotid endarterectomy were enrolled. Magnitude and phase images of five-echo 3D fast low angle shot (FLASH) were obtained using a 3T MRI, and QSM was calculated from the phase images. Conventional carotid vessel wall images (black-blood T1-weighted images [T1WI], T2-weighted images [T2WI], proton-density weighted images [PDWI], and time-of-flight images [TOF]) were also obtained. Pathological findings including intraplaque hemorrhage, calcification, and lipid rich necrosis at the thickest plaque section were correlated with relative susceptibility values with respect to the sternocleidomastoid muscle on QSM. On conventional vessel wall images, the contrast-noise ratio (CNR) between the three components and sternocleidomastoid muscle was measured respectively. Wilcoxon signed-rank test analyses were performed to assess the relative susceptibility values and CNR. RESULTS: Pathologically, lipid rich necrosis was proved in all of seven cases, and intraplaque hemorrhage in five of seven cases. Mean relative susceptibility value of hemorrhage was higher than lipid rich necrosis unexceptionally (P = 0.0313). There were no significant differences between CNR of hemorrhage and lipid rich necrosis on all sequences. In all six cases with plaque calcification, susceptibility value of calcification was significantly lower than lipid rich necrosis unexceptionally (P = 0.0156). There were significant differences between CNRs of lipid rich necrosis and calcification on T1WI, PDWI, TOF (P < 0.05). CONCLUSION: QSM of carotid plaque would provide a novel quantitative MRI contrast that

enables reliable differentiation among intraplaque hemorrhage, lipid rich necrosis, and calcification, and be useful to identify vulnerable plaques.

[27] *Polzer S, Polisenska A, Novak K, Bursa J*. **Moderate thickness of lipid core in shoulder region of atherosclerotic plaque determines vulnerable plaque A parametric study**. Medical engineering & physics 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31160196
ABSTRACT
Peak stress in the fibrous cap of atherosclerotic plaque is largely determined by the cap thickness which cannot be accurately estimated in vivo. This parametric study investigates idealized atherosclerotic plaque geometries. Finite element modeling is applied to search for larger morphological features associated with high cap stresses. By varying seven geometrical and two loading parameters, 100 3D model geometries of atherosclerotic plaques in common iliac artery were generated. In each model peak cap stress was calculated, and statistical comparison of the geometries generating the highest and lowest peak cap stresses was performed. The analysis showed that, compared to geometries generating the lowest stresses, those with high peak cap stress had a significantly lower cap thickness, higher stenosis ratio, lower relative lipid core volume, and cap shoulder radius larger than lipid core radius. High cap stress was observed for cap thicknesses up to 0.13mm. It can be concluded that vulnerable plaques contain thin fibrous cap, large stenosis ratio and only moderate small-radius lipid core which reaches the shoulder region of the fibrous cap.

[28] *Ye J, Chen X, Bao L*. **Effects of wine on blood pressure, glucose parameters, and lipid profile in type 2 diabetes mellitus: A meta-analysis of randomized interventional trials (PRISMA Compliant)**. Medicine (Baltimore) 2019; 98:e15771.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31169675
ABSTRACT
BACKGROUND: Previous studies identified conflicting results about the effects of wine intake on glucose parameters and the risk of cardiovascular diseases in type 2 diabetes mellitus (T2DM). The present study further investigated the association between wine digestion and these outcomes in T2DM patients. MATERIAL AND METHODS: A search of PubMed, Embase, and Scopus databases (up to November 2018) was performed for randomized interventional trials which evaluated the effect of wine on blood pressure (BP), glucose parameters and lipid profiles in T2DM people. We used a variety of tests: fixed and random effects models, Q Cochrane test and I index, Egger and Begg tests, forest plots, and sensitivity analysis in our study. RESULTS: A total of 9 randomized interventional studies were included in this meta-analysis. Overall, significant association between wine intake with diastolic BP (weighted mean difference [WMD] = 0.10; 95% confidence interval [95% CI]: -0.01 to 0.20, P = .03 I = 13%) and total cholesterol (TC) (WMD = 0.16, 95% CI: 0.02-0.31, P = .03, I = 6%), whereas no noticeable differences in glucose parameters, systolic BP, low-density lipoprotein cholesterol (LDLC), triglyceride (TG) and high-density lipoprotein cholesterol (HDLC) were identified between wine and controls groups (fasting glucose [FG],WMD = -0.00, 95% CI: -0.58 to 0.58; fasting insulin [FI], -0.22, -2.09 to 1.65; HbAc1%, -0.16, -0.40 to 0.07; systolic blood pressure, 0.12, -0.05 to 0.28; LDLC, -0.02, -0.25 to 0.21; TG, -0.34, -1.31 to 0.64; HDLC, 0.22, -0.08 to 0.53]. CONCLUSION: This

meta-analysis revealed that moderate wine consumption among T2DM patients could reduce the level of diastolic blood pressure and TC, but not glucose parameters and other cardiovascular risk factors.

[29] *Stampanoni Bassi M, Iezzi E, Buttari F et al.* **Obesity worsens central inflammation and disability in multiple sclerosis**. Multiple sclerosis (Houndmills, Basingstoke, England) 2019:1352458519853473.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31161863
ABSTRACT
BACKGROUND: Previous studies evidenced a link between metabolic dysregulation, inflammation, and neurodegeneration in multiple sclerosis (MS). OBJECTIVES: To explore whether increased adipocyte mass expressed as body mass index (BMI) and increased serum lipids influence cerebrospinal fluid (CSF) inflammation and disease severity. METHODS: In this cross-sectional study, 140 consecutive relapsing-remitting (RR)-MS patients underwent clinical assessment, BMI evaluation, magnetic resonance imaging scan, and blood and CSF collection before any specific drug treatment. The CSF levels of the following cytokines, adipocytokines, and inflammatory factors were measured: interleukin (IL)-6, IL-13, granulocyte macrophage colony-stimulating factor, leptin, ghrelin, osteoprotegerin, osteopontin, plasminogen activator inhibitor-1, resistin, and Annexin A1. Serum levels of triglycerides, total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) were assessed. RESULTS: A positive correlation emerged between BMI and Expanded Disability Status Scale score. Obese RR-MS patients showed higher clinical disability, increased CSF levels of the proinflammatory molecules IL-6 and leptin, and reduced concentrations of the anti-inflammatory cytokine IL-13. Moreover, both the serum levels of triglycerides and TC/HDL-C ratio showed a positive correlation with IL-6 CSF concentrations. CONCLUSION: Obesity and altered lipid profile are associated with exacerbated central inflammation and higher clinical disability in RR-MS at the time of diagnosis. Increased adipocytokines and lipids can mediate the negative impact of high adiposity on RR-MS course.

[30] *van Vollenhoven RF, Nurmohamed M*. **Methotrexate for Prevention of Cardiovascular Events**. The New England journal of medicine 2019; 380:2276-2277.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31167066
ABSTRACT

[31] *Vogel B, Claessen BE, Arnold SV et al.* **ST-segment elevation myocardial infarction**. Nature reviews. Disease primers 2019; 5:39.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31171787
ABSTRACT
ST-segment elevation myocardial infarction (STEMI) is the most acute manifestation of coronary artery disease and is associated with great morbidity and mortality. A complete thrombotic occlusion developing from an atherosclerotic plaque in an epicardial coronary vessel is the cause of STEMI in the majority of cases. Early diagnosis and immediate reperfusion are the most effective ways to limit myocardial ischaemia and infarct size and thereby reduce the risk of post-STEMI complications and heart failure. Primary percutaneous coronary

intervention (PCI) has become the preferred reperfusion strategy in patients with STEMI; if PCI cannot be performed within 120 minutes of STEMI diagnosis, fibrinolysis therapy should be administered to dissolve the occluding thrombus. The initiation of networks to provide around-the-clock cardiac catheterization availability and the generation of standard operating procedures within hospital systems have helped to reduce the time to reperfusion therapy. Together with new advances in antithrombotic therapy and preventive measures, these developments have resulted in a decrease in mortality from STEMI. However, a substantial amount of patients still experience recurrent cardiovascular events after STEMI. New insights have been gained regarding the pathophysiology of STEMI and feed into the development of new treatment strategies.

[32] *Busuioc RM, Covic A, Kanbay M et al.* **Protein convertase subtilisin/kexin type 9 biology in nephrotic syndrome: implications for use as therapy**. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31157893
ABSTRACT
Low-density lipoprotein cholesterol (LDL-C) levels almost constantly increased in patients with nephrotic syndrome (NS). Protein convertase subtilisin/kexin type 9 (PCSK9) [accelerates LDL-receptor (LDL-R) degradation] is overexpressed by liver cells in NS. Their levels, correlated inversely to LDL-R expression and directly to LDL-C, seem to play a central role in hypercholesterolaemia in NS. Hypersynthesis resulting from sterol regulatory element-binding protein dysfunction, hyperactivity induced by c-inhibitor of apoptosis protein expressed in response to stimulation by tumour necrosis factor-alpha produced by damaged podocytes and hypo-clearance are the main possible mechanisms. Increased LDL-C may damage all kidney cell populations (podocytes, mesangial and tubular cells) in a similar manner. Intracellular cholesterol accumulation produces oxidative stress, foam cell formation and apoptosis, all favoured by local inflammation. The cumulative effect of cellular lesions is worsened proteinuria and kidney function loss. Accordingly, NS patients should be considered high risk and treated by lowering LDL-C. However, there is still not enough evidence determining whether lipid-lowering agents are helpful in managing dyslipidaemia in NS. Based on good efficacy and safety proved in the general population, therapeutic modulation of PCSK9 via antibody therapy might be a reasonable solution. This article explores the established and forthcoming evidence implicating PCSK9 in LDL-C dysregulation in NS.

[33] *Tabrizi R, Ostadmohammadi V, Akbari M et al.* **The Effects of Probiotic Supplementation on Clinical Symptom, Weight Loss, Glycemic Control, Lipid and Hormonal Profiles, Biomarkers of Inflammation, and Oxidative Stress in Women with Polycystic Ovary Syndrome: a Systematic Review and Meta-analysis of Randomized Controlled Trials**. Probiotics and antimicrobial proteins 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31165401
ABSTRACT
The purpose of this systematic review and meta-analysis of randomized controlled trials (RCTs) is to determine the effectiveness of probiotic supplementation on clinical symptoms, weight

loss, glycemic control, lipid and hormonal profiles, and biomarkers of inflammation and oxidative stress in women with polycystic ovary syndrome (PCOS). Eligible studies were systematically searched from Cochrane Library, Embase, Medline, and Web of Science databases until January 2019. Cochran (Q) and I-square statistics were used to measure heterogeneity among included studies. Data were pooled by using random-effect model and expressed as standardized mean difference (SMD) with 95% confidence interval (CI). Eleven articles were included in this meta-analysis. Probiotic supplementation significantly decreased weight (SMD - 0.30; 95% CI, - 0.53, - 0.07; P = 0.01), body mass index (BMI) (SMD - 0.29; 95% CI, - 0.54, - 0.03; P = 0.02), fasting plasma glucose (FPG) (SMD - 0.26; 95% CI, - 0.45, - 0.07; P < 0.001), insulin (SMD - 0.52; 95% CI, - 0.81, - 0.24; P < 0.001), homeostatic model assessment for insulin resistance (HOMA-IR) (SMD - 0.53; 95% CI, - 0.79, - 0.26; P < 0.001), triglycerides (SMD - 0.69; 95% CI, - 0.99, - 0.39; P < 0.001), VLDL-cholesterol (SMD - 0.69; 95% CI, - 0.99, - 0.39; P < 0.001), C-reactive protein (CRP) (SMD - 1.26; 95% CI, - 2.14, - 0.37; P < 0.001), malondialdehyde (MDA) (SMD - 0.90; 95% CI, - 1.16, - 0.63; P < 0.001), hirsutism (SMD - 0.58; 95% CI, - 1.01, - 0.16; P < 0.001), and total testosterone levels (SMD - 0.58; 95% CI, - 0.82, - 0.34; P < 0.001), and also increased the quantitative insulin sensitivity check index (QUICKI) (SMD 0.41; 95% CI, 0.11, 0.70; P < 0.01), nitric oxide (NO) (SMD 0.33; 95% CI 0.08, 0.59; P = 0.01), total antioxidant capacity (TAC) (SMD 0.64; 95% CI, 0.38, 0.90; P < 0.001), glutathione (GSH) (SMD 0.26; 95% CI, 0.01, 0.52; P = 0.04), and sex hormone binding globulin (SHBG) levels (SMD 0.46; 95% CI, 0.08, 0.85; P = 0.01). Probiotic supplementation may result in an improvement in weight, BMI, FPG, insulin, HOMA-IR, triglycerides, VLDL-cholesterol, CRP, MDA, hirsutism, total testosterone, QUICKI, NO, TAC, GSH, and SHBG but did not affect dehydroepiandrosterone sulfate levels, and total, LDL, and HDL cholesterol levels in patients with PCOS.

[34] *Na EJ, Kim DJ, Kim JH, Kim GR*. **Recent trends in anti-obesity and anti-inflammatory studies in modern health care**. Technology and health care : official journal of the European Society for Engineering and Medicine 2019.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31156189

ABSTRACT

BACKGROUND: This study was planned to investigate the research trends related to naturally derived anti-inflammatory and anti-obesity components. The main purpose of this study was to find out and develop natural health cosmetic ingredients which has high effects on lipid degradation, moisturizing and elasticity enhancement. OBJECTIVE: We all hope this research provided systematic and practical data that can suggest an opportunity to further develop new products. METHODS: This is a descriptive research which classified the natural and traditional components that have important obesity management effects based on the experimental technique (in vitro and in vivo). we investigated the effects of 13 natural raw materials selected through preliminary investigation on lipid metabolism related enzyme activity. We first introduced Ainsliaea acerifolea, Onion, pear, Sanguisorba, Limonium tetragonum, Cornus walteri, Loquat, and Loquat-which have recently been shown to be effective in anti-obesity tests, and then described the research methods by showing the effects of onion extracts, Glasswort, Pine Cone (Korean white pine), Orostachys japonicus, African mangoes, Pepper, and Clathratum (sea weed), which actually had effects on anti-obesity in the in vivo experiment. RESULTS: As a result of investigating the effect of 13 natural raw materials selected through a

preliminary investigation on lipid metabolism related enzyme activity, the study found nature-derived ingredients which induce anti-inflammatory and enhance the anti-obesity enzyme activity, and ingredients showing myriads of biological activities such as anti-oxidant, body fat reduction, lowering of blood cholesterol, and weight control. CONCLUSION: In this paper, we would like to delve into the possibility of using natural components with natural lipid-lowering effect, and systematically and practically study if they can actually be helpful to develop new cosmetic products.

[35] *Maksymets T, Sorochka M, Bondarenko O et al.* **Comparison of metabolic profile of obese non-diabetic patients with coronary artery disease depending on atorvastatin dose**.
Wiadomosci lekarskie (Warsaw, Poland : 1960) 2019; 72:846-850.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=31175783

ABSTRACT

OBJECTIVE: Introduction:Cardiovascular diseases (CVD) are one of the most important medical-biological and social problems in Ukraine and in the world because coronary artery disease (CAD) is a major cause of death and disability. Overweight and obesity are risk factor of CVD and type 2 diabetes mellitus (T2DM). Although statins have been shown to be beneficial in secondary prevention of CVD in a number of trials, current reports of increased risk of T2DM with statin use raise concerns. The aim: To compare the metabolic profile and therapeutic targets of non-diabetic obese patients with CAD depending on the dose of atorvastatin. PATIENTS AND METHODS: Materials and methods: The study included 107 patients (82 men and 25 women) with CAD and abdominal obesity. Patients were divided into two groups: those taking 20 mg and 40 mg of atorvastatin daily correspondingly. Glucose, insulin, HbA1c, HOMA-IR, lipids, hs-CRP and anthropometric parameters were measured for each subject. RESULTS: Results: For patients with CAD and obesity, who had taken atorvastatin in a 40-mg dose, we observed a significant increase in insulin resistance and impaired fasting glucose. Also we found a reliable correlation between the carbohydrate and lipid spectrum. These parameters reflect the mechanism of the formation of metabolic disorders as a result of intensive statin therapy. CONCLUSION: capital ES, Cyrilliconclusions: Despite of the beneficial reductions in LDL and total cholesterol, atorvastatin treatment on a dose 40 mg resulted in significant increase of fasting glucose, insulin levels and insulin resistance pertaining to those patients.